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# ONR LONDON CONFERENCE REPORT

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PHYSIOLOGICAL SOCIETY: MILL HILL MEETING, NATIONAL INSTITUTE FOR MEDICAL RESEARCH, LONDON, 16-17 JANUARY 1970

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MAIN, GERMANY

9 APRIL 1970

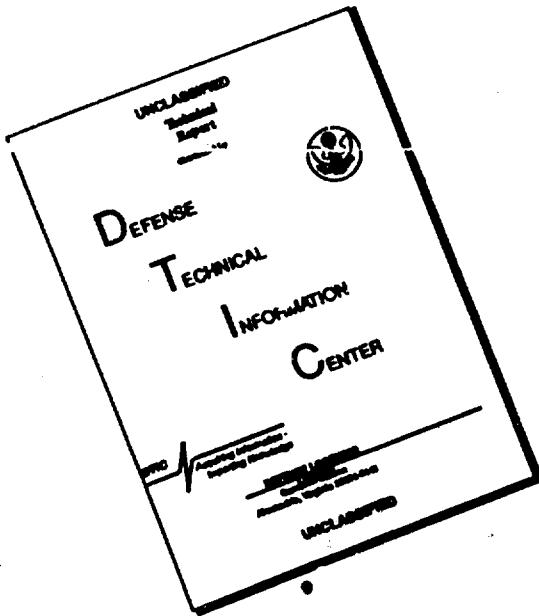
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PHYSIOLOGICAL SOCIETY: MILL HILL MEETING,  
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The Mill Hill meeting, reported here, followed the Physiological Society's usual pattern of demonstrations and brief oral communications, with precirculated abstracts that, if approved by a show of hands after presentation of each paper, will be printed later in the Journal of Physiology.

The papers covered a lot of ground but, whether by accident or by prudent selection, they can easily be classified in terms of common features of basic interest, and will be so reported in the following notes.

The two most important meetings of the academic year had yet to come: the Annual General Meeting at University College, London, 20-21 March, and the Cambridge meeting later in the spring. There was also a scientific meeting at the London Hospital Medical College, 13-14 February.

INSTRUMENTATION

Blood flow; heart rate: Two methods of measuring arterial blood velocity were discussed. A paper on hot-film constant temperature anemometry (1) reported improvements on a system previously described (2). These consisted mainly (a) in improved frequency response, so that the reliability of probe calibration by oscillation in still or moving liquids can be increased; (b) a method of calibrating for variations in blood hematocrit value; (c) introduction of two additional probes (resistance thermometers, in effect) to detect bias of temperature distribution in the blood accompanying flow reversal.

There is, of course, a great need in clinical research, and possibly in clinical practice for rapid methods of measuring blood flow without catheterization. It is hardly to be expected that these will give the detailed information yielded, in principle, by an intravascular probe; on the other hand, purely external observation as, for instance, that of the ballistocardiogram, may run into almost insuperable difficulties of interpretation if flows and their first and second derivatives are desired. A useful compromise seems to be presented by an ultrasonic probe in the megacycle frequency region with spectrographic analysis of the Doppler frequency shift arising by reflection from moving erythrocytes. In an earlier paper describing such a system (3), indeed, it was suggested that measurement of the maximum Doppler shift in a beam in line with the "main flow in the anterior bend of the aortic arch" would give the peak velocity during systolic ejection while the acceleration would be given by the first derivative. The demonstration at this meeting (4) had more to do with technical improvements and little was said about detailed analysis of the records, other than the correlation of maximum frequency shift with peak velocity. It is evident that the remainder of the record may be complicated by reflections from erythrocytes moving at an angle to the beam, from those retarded by drag at the vessel

wall, and by contributions from venous flow. However, the system in its new form seems to be compact and useful. The major improvement is in the immediate recording (in "real time"), accomplished by feeding the Doppler beat signal to 18 filters, the outputs from which go to an array of 18 electrode strips pressing upon a moving ribbon of paper which is electro-chemically darkened by the signal.

A new continuously recording cardiotachometer was demonstrated (5). The instrument reliably records average heart rates over successive 6-sec intervals. It has the advantages that (a) unlike tachometers that average the heart rate over a long period (e.g., 1 minute), it is responsive to fairly rapid changes; while (b) unlike tachometers that record the reciprocal of the interval from one beat to the next, it gives a record fairly free from rapid fluctuations. The use of the 6-sec interval necessitates a way of measuring a fraction of a beat at the end of each interval, if a range of precision better than 0 to -10 beats per minute is desired. This is done digitally, it seems, by generating a chosen number of pulses - say 10 - from the ratio of the ultimate to the penultimate complete inter-beat interval and expressing the interval between the ultimate beat and the termination of the 6-sec period as a whole number of similar pulses. This whole number divided by ten would represent a decimal fraction of an anticipated inter-beat interval, assuming the existing trend to be continued over the incomplete beat. The applicable heart rate would then be ten times the sum of the total number of complete inter-beat intervals and the fraction. The circuit is copied in Figure 1. A detailed description is promised (6).

Legend to Figure 1

Circuit diagram for digital cardiotachometer.

Harding, R.H., and Sen, R.N., 1970, ref. (5).

AND = 'AND' Gate	OR = 'OR' Gate
C = Comparator	I = Integrator
MS = Monostable	BS = Bistable
RR = Reed Relay	ms = Millisecond

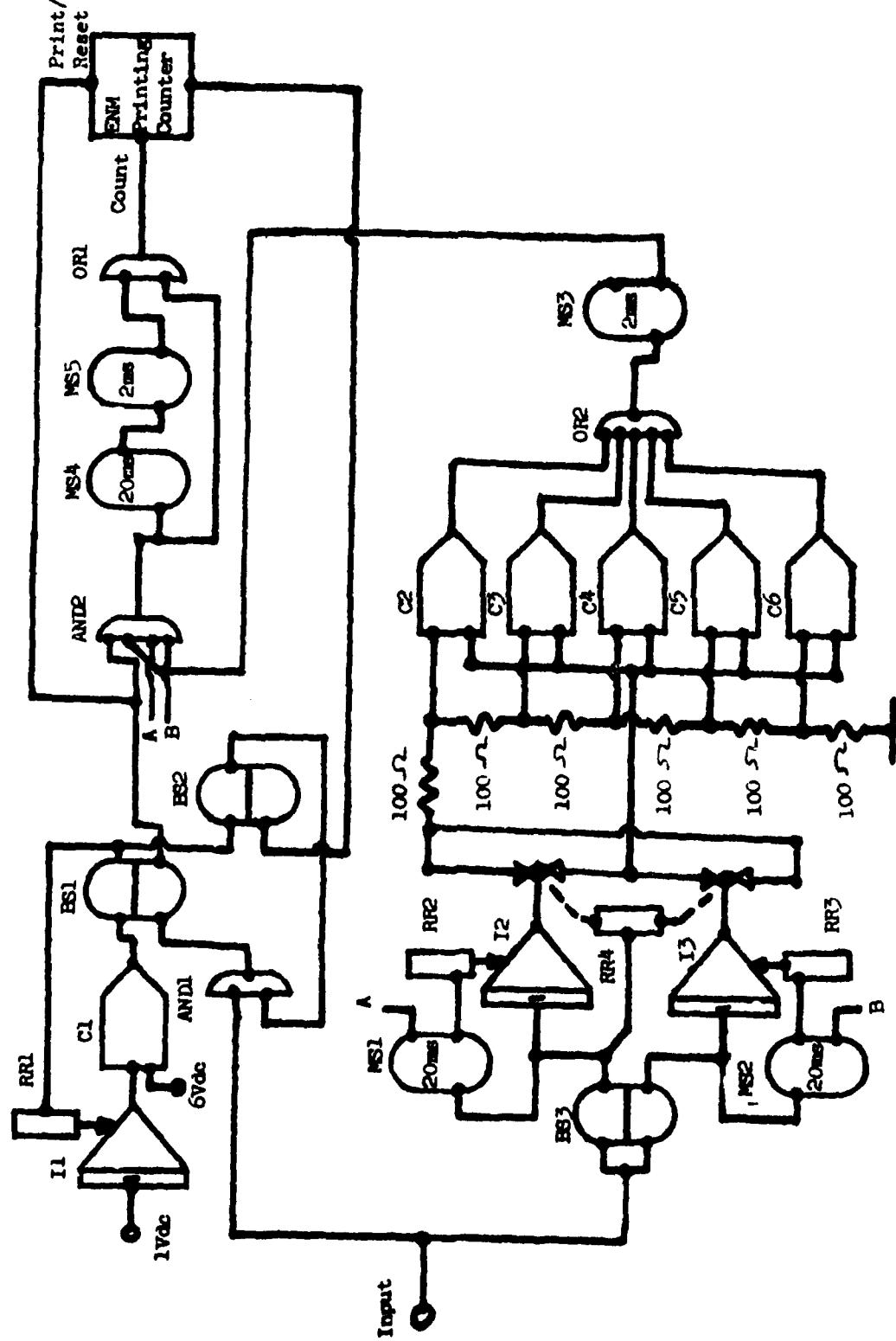
Sec. Tieser

### Counter Inhibitor

### Frequency Doubler

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3



Analogue/Digital Converter

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Ergonomics: An Automobile equipped for physiological studies (7): The car is equipped with apparatus for recording the electrocardiograms and heart rates of driver and passenger under various conditions. The ECG can be displayed directly or can be used as a trigger from which a trace of reciprocal heart rate is derived. Driving conditions are represented by speed and acceleration recordings, supplemented by four event markers operated by the observer.

In illustration of results obtained, the percent increase in heart rate was shown as a function of acceleration for teenage and for 'experienced' (35 - 40 years) drivers. The teenage response was far less than that of the older group. The same was true for deceleration but the functional relationship appeared to be different.

The car was designed at Mill Hill, in the Division of Human Physiology under O. G. Edholm, whose name has long been associated with ergonomics. Ergonomics research has a prominent place in British applied physiology and, as a recent review shows (8), is also receiving increased attention in France.

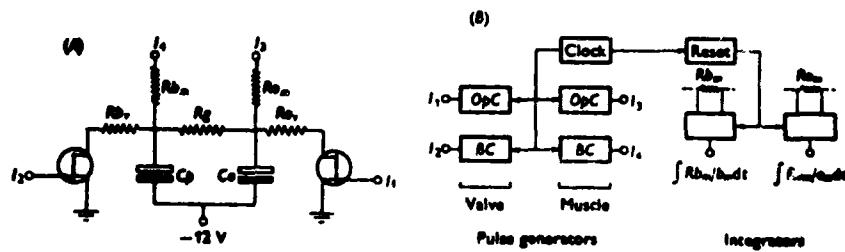
#### MODELS

Cardiac Fluid Dynamics: Increasing use is being made in biology of models and analogs in the hope that they will illuminate the working details of systems that seem otherwise to be intractable, from bio-chemical reaction sequences to the mammalian electrocardiogram. They vary in sophistication, but most of them show some advance on the work of a Cambridge mathematician around 1910, referred to by A. V. Hill in his third Bayliss - Starling Memorial Lecture (9): "...he once constructed a working model of a spermatozoon which swam very well in glycerol. Its chief defect was that it did not go as fast as he calculated; but that was due to its having a body to house its motor. The calculation referred to a disembodied tail."

The advantages of models for studying the fluid mechanics of heart action were nicely illustrated at the meeting by two papers. In one (10), direct observation of anesthetized animals was used with both cine-angiography with a radio-opaque dye and endoscopic cine-photography of small bubbles. In the other (11) a model left ventricle was described. The model incorporated a tricuspid aortic valve with sinuses and other types of mitral valve. It was placed in a rigid box filled with water so that filling and emptying of the model could be brought about by pumping water out of, and into, the box. The beating heart and the model seemed to give quite similar results, notably in showing basic stability of flow except at certain times, when strong vortices are created, with the effect of holding the cusps of the mitral valve in a stable position and otherwise governing valve dynamics. The model approach would seem to be capable of providing a lot of detailed information with considerably less expenditure of effort than the rather elaborate arrangement needed for direct observation.

The mitral valve model just mentioned was developed in the Department of Engineering Sciences, University of Oxford. I am indebted to Mr. T. Wernecke of this office for drawing my attention to current activities of this kind in two other laboratories. At the Aerodynamisches Institut der Rheinisch-Westfälischen Technischen Hochschule, Aachen, Professor A. Naumann (12) is using model systems to study the fluid dynamics of cardiac prostheses with special reference to the effects of abnormal flow relationships upon hemolysis and thrombus formation. Also, in the Department of Aeronautics at Imperial College, under Professor P. Owen, there is a Subdepartment of Physiological Flow about which we have no further knowledge.

Respiratory mechanics of fish: Other problems in fluid mechanics exist in understanding the respiratory system of fish: pressure changes have been recorded in the buccal and opercular cavities, but the internal processes from which these pressure profiles result are not understood quantitatively, although the anatomical arrangement is known. Thus, it is fairly easy to build a model in which the components can be adjusted so as to reconstruct the recorded pressure relationships. Hydraulic models exist. The new electronic analog model (13) appears to have some advantages in flexibility, with twenty adjustable variables. The circuits are shown in Fig. 2.



(from Hughes and Woakes, ref. 13)

Fig. 2.

Fig. 2: (A) Basic circuit representing the double-pump mechanism.  $R_{b_m}$ ,  $R_{o_m}$  are the resistance to water flow when the buccal and opercular valves (Fet's) are open:  $R_g$  is the gill resistance;  $R_{b_m}$ ,  $R_{o_m}$  are the resistances associated with the muscle drive system;  $C_p$ ,  $C_o$  are capacitors representing the elasticity of the two cavities;  $I_1$ - $I_4$  are the inputs from the pulse generators shown in Fig. 2B.

(B) Block diagram of the valve and muscle driving circuits for the opercular and buccal cavities (OpC, BC). Also shown are the two integrators and the circuit which resets them at the beginning of every breathing cycle.

#### CIRCULATION, RESPIRATION

Carbon dioxide as pulmonary vasodilator: Measurements (14) of mean pulmonary artery pressure in isolated blood-perfused rat lungs at constant flow rate showed that if vasoconstriction is produced by anoxia, addition of carbon dioxide to the ventilating gas causes dilatation. In absence of anoxia,  $\text{CO}_2$  caused vasoconstriction or was without effect, depending on conditions. The authors find that their results suggest a variable dilator effect of  $\text{CO}_2$ , or a variable balance between a constrictor and a dilator action. This finding is reminiscent of the variable effect of  $\text{CO}_2$  on local cerebral blood flow noted by Sem-Jacobsen of Oslo, working under contract with the US Army (15, 16).

Osmotic effects on pulmonary vasculature: A paper from the University of Oslo (17) described a rather curious result that may be significant during muscular exercise. Isolated, ventilated rabbit lungs were perfused with plasma. Increase of the plasma osmolarity with sodium chloride, urea or ethylene glycol caused a decrease of resistance to blood flow and a loss of weight. The former is attributed to dilatation of "resistance" vessels, and the latter principally to a constriction of "capacitance" vessels, although one might imagine it to be due, rather, to osmotic withdrawal of water from the vascularized tissues, the effect being greatest with sodium chloride and least with ethylene glycol. This point was not clarified, nor did it seem that any measurements of reversibility had been done.

Effects of aerodynamic resistance in the respiratory tract: work from the Pneumoconiosis Unit of the Medical Research Council: A demonstration (18) and a communication (19) dealt with the effects produced when one breathes through an external resistance. It must be presumed that the objective is to find a correlation between these effects and the presence or absence of internal respiratory impairment in certain diseases. This idea met with some scepticism on the ground that an external resistance by no means duplicates the stresses produced by internal impairment, which may involve the use of different muscles and quite different sorts of change in the distribution of blood in the pulmonary vessels. The demonstration had to do with the ability to detect the presence of a small external viscous resistance. The proportion of false alarms (i.e., "detecting" the resistance when it was absent) was interpreted in terms of a hypothetical Gaussian distribution of internal "noise," and the proportion of correct answers in terms of a similar distribution of noise plus signal. These values were then converted into "sensitivity" and "decision bias," the latter representing an eagerness (or reluctance) to give positive reports. Without further information it is not quite clear how this simultaneous solution for two quantities is derived. A simple approach would enable solutions to be obtained for the threshold and the signal intensity from tables of integrals of the normal

distribution function, but bias on this basis would be included within an increase or decrease of the threshold intensity. Greater familiarity with communication theory would no doubt clarify this.

The companion investigation had to do with changes in rate of breathing (ratio of minute volume to tidal volume) when inspiration is impeded by an external elastic load during performance of progressive muscular exercise. A marked tachypnoea developed in most subjects. The mechanism is obscure, and no dependence could be noted on the detection threshold or on several other properties, including specific airway conductance and degree of neuroticism.

#### MEMBRANES, SECRETIONS

Cerebrospinal fluid: The ionic compositions of cerebrospinal fluid and of the brain extracellular fluids are kept remarkably constant and are comparatively unresponsive to changes in the circulating blood. Concentrations of specific ions may even change in contrary directions in csf and plasma, for example, in response to large decreases or increases of blood sodium (20). These relationships are poorly understood and asymmetric behavior is often seen. The paper on this subject (21) dealt with the claim that the potential difference between blood and csf varies with csf potassium concentration, but not with blood potassium. The results presented failed to confirm this asymmetry with respect to potassium; the cerebrospinal fluid became more positive as the plasma potassium was increased (presumably at constant pH) and the relationship between the csf - blood potential difference and  $\log [K']$  (plasma) -  $\log [K']$  (csf) was linear. The potential difference also varied linearly with arterial pH at constant plasma  $[K']$ , the csf becoming more positive at low pH. The slope of the line was decreased by hyperkalaemia.

Intestinal absorption of amino acids and oligopeptides increased in semi-starvation: The paper (22) described measurement of the rate of absorption of L-methionine and L-methionyl-L-methionine in jejunal loops of normal and semi-starved growing rats. The control rats presumably continued to grow normally; the semi-starved rats received a diet reduced sufficiently to keep the body weight constant. The oligopeptide was under all conditions absorbed more rapidly than the free amino acid. The data showed that over the concentration range studied, 100 to 300 mM/l methionine was absorbed significantly more rapidly in the starved animals, whereas the oligopeptide showed the same tendency but to a statistically significant degree only at 50 mM/l (range studied, 50 to 150 mM/l). The authors conclude that "the stimulating effect of short-term starvation or intestinal transport applies to oligopeptide as well as free amino acids." The data as presented would seem to give only marginal justification for this unqualified statement, but it is of interest that the results were expressed per centimeter length of a jejunum, and that the weight of jejunum per centimeter, wet or dry, decreased considerably in the semi-starved animals. Obviously, as the authors note, the effects of starvation are accentuated if this is taken into account. This can be seen from Table 1, calculated from numbers given in the abstract for 100 mM/l.

TABLE 1

Rate of absorption of methionine and its dipeptide from  
jejunal loops of rat

Data of Crampton, Lis, and Matthews, 1970, ref (22).

	Starved	Semi-starved
Dry wt., g. per cm.	0.028	0.017
Methionine absorption rate:		
per cm.	2.00	2.54
per g. dry wt.	71	149
Methionyl methionine absorption rate:		
per cm.	2.69	2.99
per g. dry wt.	96	176

This would seem to show that if absorption is a simple permeability phenomenon - which is unlikely - then the permeability of the jejunum is little affected by loss of dry weight. If, on the other hand, it is an active process, then the solids remaining after starvation are more active per gram than the solids in the normal jejunum. It would be interesting to know whether this is due to the loss of inert material or whether there is actually an increase in the specific activity of a pump. The net result in total uptake, however, is the comparatively small increase noted when the results are expressed per centimeter length, because semi-starvation produced no change in the total length of the gut.

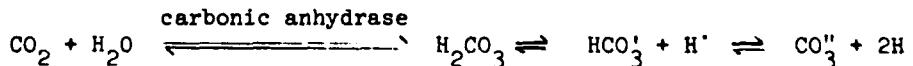
Indirect evidence for association of renal oxygen uptake and sodium transport: Because newborn animals are said to be less able than adults to dilute and concentrate their urine, it was assumed (23) that their sodium transport rates would be low; and if oxygen uptake is involved, the oxygen consumption of kidney slices from newborn animals would be less than that from adults. Taking advantage of the report that the renal function of the guinea pig approaches that of the adult more rapidly than that of the rat, the oxygen uptake and glycolysis of kidney slices (cortex and medulla) were compared in adult and newborn rats and guinea pigs. The  $QO_2$  of the newborn guinea pig kidney slices reached the adult value in less than 24 hours, while the values for the newborn rat remained somewhat lower than the adult value after 21 days. Such results are at best "suggestive" and work of this kind can no longer compete successfully with the rapid advance of micro techniques for determining the properties of the individual secretory elements in vivo.

Impermeable "silvery" layers in fish: A metallic appearance is characteristic of most fish, and everyone has noticed that some of the internal organs show the same property. The authors of this paper (24) ask why these internal structures should be silvery when, unlike the external scales, they have no obvious function as reflectors of light. One answer seems to be that the silvery layers, which are composed largely of guanine - presumably in the form of a dense ordered array of small crystals - are formed in places where a barrier to the permeation of gases is needed. An example is the swim bladder, and it was shown in the communication that removal of the silvery layer from the swim bladder of the conger eel, leaving only an epithelial layer, caused permeabilities to nitrogen, oxygen and carbon dioxide to increase some fortyfold, approaching values characteristic of connective tissue. It was shown also that the rete mirabile, an elaborate network of blood vessels with a counter-current arrangement somehow involved in the filling of the swim bladder, is equipped with two silvery layers which ensure that gas cannot by-pass the system.

The formation and structure of the silvery layers would be worth closer examination, and the early papers mentioned in the abstract (25, 26, 27) may contain useful information.

The paper was given by a co-worker. The senior author, E. J. Denton, has been for some years Physiologist at the Marine Biological Laboratory, Plymouth. He is known for his ingenious study of the buoyancy of the squid and is one of the more promising and imaginative of British physiologists.

Effect of a carbonic anhydrase inhibitor on eggshell formation: It has been thought that the deposition of calcium carbonate in eggshell formation occurs by a process similar to that resulting in acidification of the urine. The hydration of metabolic carbon dioxide produces carbonic acid, the ionization of which is promoted by the combination of protons with hydroxyl ions secreted by the shell gland. The residual intra-cellular protons enter the blood to produce the metabolic acidosis characteristic of the period of eggshell formation, while the carbonate ions remain in the oviduct to combine with calcium:



It was known that inhibitors of carbonic anhydrase inhibit shell deposition and in this communication (28) it was shown that one of these, acetazolamide, also greatly decreases the fall in intracellular pH during shell deposition. The work involved direct measurement of extra-cellular pH and indirect measurement of intra-cellular pH. The latter was calculated from the external concentration of a substance, dimethyloxazolidinedione, the unionized molecules of which cannot pass the cell membrane, combined with values of the extra-cellular volume in which known amounts of the substance had been dissolved. The results do not conclusively prove that carbonic

anhydrase-catalyzed hydration of  $\text{CO}_2$  is the rate-limiting process, because the inhibitor is not specific and, like sulfanilamide, may be acting directly upon a metabolic pump.

Removal of ions from hypertonic plasma by the salt glands of geese: The marine teleost fish are well known to maintain a constant internal osmolality close to that of freshwater fish by branchial excretion of a concentrated salt solution. Birds in marine habitats perform the same task by excreting salt through a nasal salt-gland. The glandular circulation is rather inaccessible, and indirect methods must be used to study the effectiveness of this mechanism. In this work (29) cardiac output was monitored continuously in  $\text{NaCl}$ -loaded geese, and when secretory activity had reached its highest rate,  $\text{Rb}^{86}\text{Cl}$  was injected, the animal killed 1 minute later, and (one assumes) the proportion of the cardiac output reaching the salt gland determined by extracting the  $\text{Rb}^{86}\text{Cl}$  from the gland. Some numbers reported in the paper are collected in Table 2. The most interesting points, perhaps, are (i) that cardiac output and gland blood flow increase considerably with blood hypernatremia; (ii) that the preferential extraction of ions, vis a vis water, from the arterial plasma is clearly demonstrated; (iii) that rates of secretion are positively correlated with plasma salt concentrations but not with blood flow.

This work was done at the Institute of Animal Physiology, Babraham, Cambridge. The work of the Institute has broadened considerably in scope and technical resourcefulness under the directorship of R. D. Keynes and must be considered among the first three or four laboratories of Physiology in the UK.

TABLE 2

Performance of salt-gland of goose

Data of Hanwell, Linzell and Peaker (29)

NaCl injected i.v. (18 ml/kg)	0.154 M	0.5 M
Salt gland blood flow	$0.827 \pm 0.219$	$11.63 \pm 1.33 \text{ ml/g tissue} \times \text{min.}$
Cardiac output	$26.3 \pm 2.2$	$36.0 \pm 2.3 \text{ ml/100 g} \times \text{min.}$
Nasal fluid secreted in 30 min.	(0?)	$0.181 \text{ to } 1.33 \text{ ml/g tissue} \times \text{min.}$
Percent extraction of ions from arterial plasma (average and range)		
$\text{Na}^+$	-	24.9 (4.5 to 52.5)
$\text{K}^+$	-	22.8 (2 to 48)
$\text{Cl}^-$	-	34.1 (2 to 81)
$\text{H}_2\text{O}$	-	9.5 (2 to 21)

## Correlation coefficients:

Rate of secretion and  $\text{Na}^+$  concentration:  $r = 0.7619. P < 0.05$

Rate of secretion and  $\text{Cl}^-$  concentration:  $r = 0.8369. P < 0.02$

Rate of secretion and blood flow:  $r = -0.0808$

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PRESERVATION OF TISSUES BY DEEP COOLING

Preservation of excitability of smooth muscle by deep cooling in aqueous dimethylsulfoxide: It is generally held that tissue injury during deep cooling and re-warming results largely from the formation of ice crystals, although concentration of solutes as ice is formed may contribute. The success that has resulted from the addition of penetrating solutes such as glycerol and dimethylsulfoxide (DMSO) before freezing is due partly to the lowering of the temperature at which ice crystals can form and to a tendency of such mixtures to supercool. There are limitations; if enough DMSO is added to prevent crystallization at the low temperature wanted for tissue preservation, it will produce undesirable osmotic displacements or toxic effects at room temperature before cooling is started; and if cooling is started too soon, the DMSO will not have penetrated the cells and intra-cellular crystallization may occur, with resultant injury to cell membranes. Secondly, upon thawing, the cells loaded with glycerol or DMSO are osmotically unstable because of the disparity between the permeability of the cells for water and for the added solute, so that attempts to restore a physiologically normal aqueous environment may result in lysis.

The work demonstrated, without verbal or printed communication (30) seemed to be based upon (i) the idea that injury arising from the use of too high an initial concentration of DMSO might be avoided by loading the muscle with increasing concentrations of DMSO during step-wise cooling, and (ii) the realization that a knowledge of the kinetics of penetration of DMSO is basic to the success of such a stratagem. Accordingly, rather elaborate measurements of the diffusion coefficient of DMSO in muscle, and its temperature dependence, were made by first loading the muscle with DMSO containing radioactive DMSO, placing it then in an unlabeled DMSO of the same concentration and measuring the rate of entry of radioactive material into the ambient solution. With this information on hand, it was possible to set up a routine by which muscles were equilibrated at room temperature with a given DMSO solution, cooled to a temperature above the ice point, re-equilibrated with a more concentrated solution, cooled to a still lower temperature, and so on. Experiments done at each of these stages, followed by warming, removal of DMSO, and measurement of excitability, gave evidence of success in restoring the excitability of muscles cooled to below  $-22^\circ\text{C}$ . At  $-79^\circ\text{C}$  the restoration was imperfect, for reasons not yet understood.

Dr. Audrey U. Smith, in whose laboratory the work was done, said that similar studies were being done with cartilage, with somewhat different

results. B. Elford received his PhD degree for the work on taenia coli and hopes now to get a more basic understanding of membrane phenomena by working in Danielli's laboratory in Buffalo, N. Y.

#### CENTRAL NERVOUS SYSTEM; TOXINS

Experiments with bacterial toxins: The bacterial toxins are being used increasingly in neurophysiological research. A paper given last June (31) noted differences in the rate of development of histological changes in a "slow" and a "fast" muscle after injection of botulinum toxin, and these findings were taken as further evidence for differences in the innervation of slow and fast muscles. At the Mill Hill meeting work on demyelinating lesions produced by diphtheria toxin was described (32). Localized cordal lesions were produced with small injections of toxin, and changes of conduction were studied by comparing the conduction velocity and refractory period of transmission through the affected region with values obtained in the neighboring areas. Antidromic impulses were picked up with microelectrodes on single afferent fibers from the intercostal muscles. Velocity was reduced by more than 50% in the demyelinated zone and the average refractory period was increased from 0.84 msec to 1.70 msec.

Cerebral ischemia: Another paper (33) dealt with the rates at which cerebral ischemia produces neuronal alteration and mitochondrial swelling in the rat and the primate brain. The rates of response to arterial hypotension, air embolism and hypoglycemia were found to be the same in the two genera and the conclusion was drawn that the changes observed are primary consequences of cellular metabolic failure. This work came jointly from the MRC Neuropsychiatry Unit, Carshalton, Surrey, and the Institut de Neurophysiologie et de Psychophysiologie (Département de Neurophysiologie Appliquée), CNRS, Marseille. Research of this kind would be of interest to the Army. Contacts have already been established with the French Institute by way of a contract on a different subject with Dr. Chalazonitis of the Département de Neurophysiologie Cellulaire (34). The organization of the Institute has been described by Glinos (35).

Inhibition; potentiation; central regulation of breathing: Other neurophysiological papers were more specialized, one (36) on suppression of excitability of cerebellar Purkinje cells, another (from the University of Oslo) (37) on prolonged potentiation of monosynaptic response in the hippocampus by means of tetanic stimuli. Respiratory physiology was represented by a paper (38) describing the stereotaxic exploration of the chicken brain stem, which revealed the existence of a pneumotaxic center apparently homologous with the pneumotaxic center in the mammalian pons.

#### SPECIAL SENSES

Cochlear frequency response curves: work from the Department of Communication, University of Keele: At the November 1969 meeting of the Physiological Society, it was shown (39) that while the threshold - frequency

curve for the basilar membrane in the guinea pig ear is flat and monotonic between 1 and 20 kHz, the response areas obtained from single fibers of the cochlear nerve are quite narrow. Evidently the flat response of the basilar membrane is somehow sharpened within the cochlea, unless indeed the measured flat response curve of the basilar membrane is a surgical artifact. In the recent communication (40) further experiments were described in which responses to white noise and to pure tones were compared. The analysis - which I do not understand - was said to confirm the idea that the cochlea acts as a linear narrow-band filter.

#### TISSUE TRANSPLANTATION

Absence of lymphatic drainage of skin homografts: Chemical or thermal injury causes intracellular enzymes to appear in the lymph. Immunological insult, such as is produced by skin homografts, on the other hand, does not affect the composition of the lymph in this manner. The paper on this subject (41) described experiments in which connections between the graft area and the circulating blood and the lymphatics were examined by using Evans Blue as tracer. It was found that the rejection process prevents the development of a lymphatic connection with homografts, whereas with autografts such connections were established. This finding is being followed up by inducing homograft acceptance with drugs and thus being able to initiate the rejection process at will.

#### NUTRITION. OBESITY

Postprandial metabolic rise and "plumpness": According to this study (42) the rise in metabolic rate following a meal is very much the same for "thin" and "plump" persons (classified according to the percentage of body fat), and is not increased in either group by postprandial exercise. Thus, metabolic response would seem to play no part, contrary to other claims, in controlling obesity. It was objected, however, that the experimental subjects were normal persons, and that different results might have been obtained in cases of true obesity. This paper was of interest in view of a recent discussion with Dr. Solomon H. Blondheim (43) who combines (i) physiological, and (ii) psychiatric approaches to the problem of obesity. (i) One physiological approach is considerably more specific than that used in the above study since rates of fat synthesis, as indicated by blood lipid levels, are used rather than overall metabolic rate. The influence of environmental temperature has been studied in some detail (44); temperature and lipid synthesis were found to be inversely related. (ii) The psychiatric factor is stressed (43) and methods of personnel screening are being developed in order to distinguish between compulsives who can control their obesity and the incurables for whom obesity is a psychological necessity. Seen in the light of this approach, the investigation reported on Mill Hill is rather trivial, although necessary in order to settle a controversy. On the other hand, the psychological approach may be invaluable in eliminating potentially obese candidates for military assignments in which obesity cannot be tolerated.

COMMENT

It has been interesting to realize, after a long absence from ordinary physiology, that most of the problems still being investigated were equally prominent twenty or thirty years ago. Each meeting of the Physiological Society, modest in proportions and yet representative in character, provides a sort of reduced image of current physiological research. The picture can be taken in at a glance. This is not attributable only to the small size of the meetings; largely it is due to the deliberate efforts of the Society to avoid the various background noises that obscure so much of American science. One sees evidence of this concern for clarity in many of the details of the Society's activities: the insistence on limitation of the proceedings so as to avoid dividing the meetings into simultaneous sessions; the preprinting of the communications in the same pleasing format, and on paper of the same good quality, that one finds in the Journal of Physiology; the friendly but critical manner in which the communications, mostly very well presented, are received by the Society; the pains evidently taken to make the demonstrations intelligible and informative; and the lucidity with which all the business of the Society is announced in printed circulars.

As for the scientific content of the Society's activities, the problems, as noted already, have not changed fundamentally over many years. To say this is in no way to imply stagnation. Quite the contrary: the problems are still with us because they are fundamental, and the fact that one is constantly aware of them during these meetings is proof that they have not been abandoned in favor of easy and trivial successes. The objectives of the Society are of course limited in a sense: largely to physiology as an experimental science at the level of the whole organism. With this self-imposed limitation it is natural that some of the more spectacular recent advances in science should not appear explicitly in the pages of the Journal; but it is obvious enough, and it is another sign of vitality, that exploitation of these advances when they are applicable is prompt and sophisticated. This applies as much to electronics as to information theory, irreversible thermodynamics, molecular biology and polymer chemistry, and the specialized terminologies of these disciplines will often be found in papers on renal physiology, visual acuity, pituitary function, electrocardiography or the rheology of blood. Within the definition of physiology, moreover, the scope of the Society is as broad as could be wished; it has never come under the domination of a particular group, whether clinical, applied, mammalian, electro, neuro, cellular, or even general. Editorial policy, clearly, is to accept the fact that crabs and seagulls are just as respectable as objects of physiological research as hospital patients or coal miners, and often far more informative.

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